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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,625	11/02/2006	Stephen J. Klaus	FP0617 US	7369

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EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
01/31/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,625	KLAUS ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12-16,48 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 12-16 and 48-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/15/10 has been entered.

Claims 2-11, and 17-47 have been cancelled. Claims 1, 14-16 and 48-49 have been amended. Claims 1, 12-16 and 48-49 are pending and are under examination.

Claim Rejections Withdrawn

The rejection of claims 1, 12-16, and 48-49 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to the claims.

The rejection of claim 27 under 35 U.S.C. 102(e) as being anticipated by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 is withdrawn in view of the cancellation of the claim.

The rejection of claim 27 rejected 35 U.S.C. 103(a) as being unpatentable over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 in view of Perrine et al. WO 93/18761, 1993, cited in IDS is withdrawn in view of the cancellation of the claim.

The rejection of claims 28-31, 33 and 36 under 35 U.S.C. 103(a) as being obvious over Bohmer et al WO 01/12784 A1 22 February 2001, cited previously in view of Skarpidi et al. Experimental Hematology 31 (March 2003) 197-203 as evidenced by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 is withdrawn in view of the cancellation of the claims.

The rejection of claim 32 under 35 U.S.C. 103(a) as being obvious over Bohmer et al WO 01/12784 A1 22 February 2001, cited previously and Skarpidi et al. Experimental Hematology 31 (March 2003) 197-203 and as evidenced by Klaus et al. US 2003/0153503

published Aug 14, 2003, filed Dec. 6, 2002 as applied to claims 28-31,33 and 36 above, further in view of Perrine et al. WO 93/18761, 1993, cited in IDS is withdrawn in view of the cancellation of the claim.

Claim Rejections - Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1, 12-13, 15-16, and 48-49 under 35 U.S.C. 102(e) as being anticipated by Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002. as evidenced by Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203, cited previously) is maintained

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are drawn to a method for treating hemoglobinopathy in a subject, the method comprising administering to the subject in need thereof a compound that inhibits hypoxia-inducible factor (HIF) prolyl hydroxylase wherein the compound increases expression of the

gene encoding γ-globin in a bone marrow derived cell a hematopoietic stem cell or a blast – forming unit erythroid cell thereby treating the hemoglobinopathy in the subject.

Klaus et al discloses a method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy such as abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80) comprising administering to a subject in need thereof a compound which inhibits HIF prolyl hydroxylase (see p. 2 paragraph 17-18) wherein the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic inhibits (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron (see paragraph 110).

The hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14) inherently have the property of increasing expression of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells and thus administering the hydroxamate iron chelator or structural mimetic of 2 oxoglutarate increases the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by bone marrow derived cells or hematopoietic stem cells or blast forming erythroid cells. Klaus et al teaches the same active method steps of administering an iron chelator and structural mimetic of 2-oxoglutrate to a subject in need thereof in order to treat a hemoglobinopathy. The wherein clause " wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell a hematopoietic stem cell or a blast –forming unit erythroid cell" merely expresses the intended result of the positively recited step of administering the inhibitor of HIF prolyl hydroxylase to a subject and is not given any weight. See MPEP 2111.04. Moreover, as evidenced by Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203, cited previously) one of skill in the art would have recognized that the hydroxamate iron chelators (which are inhibitor of hypoxia inducible factor prolyl hydroxylase as taught by Klaus et al) have the inherent property of being able to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin as Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression (see p. 202 column 1 first incomplete paragraph and last bridging paragraph to column 2).

Applicants' arguments:

Klaus et al. discloses methods for increasing endogenous erythropoietin and for treating anemia. (See, e.g., paragraphs [0017] and [0018].) Anemic conditions are defined to include "any condition, disease, or disorder associated with anemia." (See, e.g., paragraph [0080].) However, Klaus et al does not disclose use of a compound that "increases expression of the gene encoding y-globin in a bone marrow-derived cell, a hematopoietic stem cell, or a blast-forming unit erythroid cell" as recited in amended claim 1. Therefore, Klaus et al. does not set forth each and every element recited in claim 1, and does not anticipate claim 1 for at least this reason. Accordingly, claim 1, and claims 12, 13, 15, 16, 48 and 49, which depend directly or indirectly from claim 1 are not anticipated by Klaus et al.

Response:

Applicants' arguments are carefully considered but are not persuasive. Although, Klaus et al does not specifically disclose the inherent functioning of hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate that inhibits HIF prolyl hydroxylase i.e. increasing expressing of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells, Klaus et al discloses that they are inhibitors of HIF prolyl hydroxylase and teach a method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy such as abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80) with said compounds. Klaus et al discloses the same HIF prolyl hydroxylase inhibitors as claimed for treating the same condition in the claims i.e. hemoglobinopathy.

The ability of the hydroxamate or structural mimetics of 2 oxo-glutarate which are inhibitors HIF prolyl hydroxylase to increase expression of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cell is inherent to the hydroxamate or structural mimetics of 2 oxo-glutarate. Moreover, Klaus et al teaches the same active method steps. The wherein clause " wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell a hematopoietic stem cell or a blast –

forming unit erythroid cell" merely expresses the intended result of the positively recited step of administering the inhibitor of HIF prolyl hydroxylase to a subject and is not given any weight. See MPEP 2111.04. Furthermore, when a claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated. In re May, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978) (Claims 1 and 6, directed to a method of effecting nonaddictive analgesia (pain reduction) in animals, were found to be anticipated by the applied prior art which disclosed the same compounds for effecting analgesia but which was silent as to addiction. The court upheld the rejection and stated that the applicants had merely found a new property of the compound and such a discovery did not constitute a new use. See MPEP 2112.02. Moreover, as evidenced by Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203, cited previously) one of skill in the art would have recognized that the hydroxamate iron chelators (which are inhibitor of hypoxia inducible factor prolyl hydroxylase as taught by Klaus et al) have the inherent property of being able to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin and Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression and Skarpidi et al suggest that these hydroxamate iron chelators for treatment of beta thalassemia and sickle cell disease (see p. 202 column 1 first incomplete paragraph and last bridging paragraph to column 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1, 12-16, and 48-49 under 35 U.S.C. 103(a) as being unpatentable over Klaus et al. US 2003/0153503 published Aug 14, 2003, filed Dec. 6, 2002 in view of Perrine et al. WO 93/18761, 1993, cited in IDS as evidenced by Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203, cited previously is maintained.

The claims are drawn to a method for treating hemoglobinopathy in a subject, the method comprising administering to the subject in need thereof a compound that inhibits hypoxia-inducible factor (HIF) prolyl hydroxylase wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell a hematopoietic stem cell or a blast – forming unit erythroid cell thereby treating the hemoglobinopathy in the subject.

Klaus et al discloses a method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy such as abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80) comprising administering to a subject in need thereof a compound which inhibits

HIF prolyl hydroxylase (see p. 2 paragraph 17-18) wherein the compound is an hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14). Said 2 oxoglutarate mimetic inhibits (HIF) prolyl hydroxylase competitively with respect to 2 oxoglutarate and non-competitively with respect to iron (see paragraph 110).

The hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate (paragraph 110 p. 14) inherently have the property of increasing expression of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells and thus administering the hydroxamate iron chelator or structural mimetic of 2 oxoglutarate increases the proportion of fetal hemoglobin relative to non-fetal hemoglobin produced by bone marrow derived cells or hematopoietic stem cells or blast forming erythroid cells. Klaus et al teaches the same active method steps of administering an iron chelator and structural mimetic of 2-oxoglutrate to a subject in need thereof in order to treat a hemoglobinopathy. The wherein clause " wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell a hematopoietic stem cell or a blast –forming unit erythroid cell" merely expresses the intended result of the positively recited step of administering the inhibitor of HIF prolyl hydroxylase to a subject and is not given any weight. See MPEP 2111.04. Moreover, as evidenced by Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203, cited previously) one of skill in the art would have recognized that the hydroxamate iron chelators (which are inhibitor of hypoxia inducible factor prolyl hydroxylase as taught by Klaus et al) have the inherent property of being able to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin as Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression (see p. 202 column 1 first incomplete paragraph and last bridging paragraph to column 2).

Klaus et al does not teach that the hemoglobinopathy is β^o - or β^+- β thalassemia.

Perrine et al teach other types of β thalassemia such as βo - or β^+-. See p. 2 lines 16-30.

It would have been prima facie obvious to one of ordinary skill in the art to have used the method of Klaus et al to treat other β thalassemia disorders such as β^o - or β^+-, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is that Klaus et al teach that hemoglobinopathy such as abnormal hemoglobin such as beta thalassemia

can be treated by administering HIF prolyl hydroxylase inhibitors such as hydroxamate or structural mimetics of 2 oxo-glutarate.

Applicants' arguments:

The Examiner characterized Klaus et al. as disclosing "a method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy." (Office Action, section 11, page 7.) As noted above, Klaus et al. does not disclose treatment of a hemoglobinopathy in a subject as recited in the instant claims, using a compound that increases expression of the gene encoding γ-globin in a bone marrow-derived cell, a hematopoietic stem cell, or a blast-forming unit erythroid cell. Similarly, Perrine fails to provide any disclosure relating to the use of such compounds. The Examiner stated that Perrine et al., teaches "other types of β thalassemia such as βo - or β^{+}-. and thus makes it "prima facie obvious to one of ordinary skill in the art to have used the method of Klaus et al. to treat other β thalassemia disorders ...." (Office Action, section 11, page 8.) However, as noted previously, the present claims require the use of a compound that capable of increasing expression of the gene encoding γ,-globin in a bone marrow-derived cell, a hematopoietic stem cell, or a blast-forming unit erythroid cell. As neither Klaus nor Perrine, singly or in combination, teach the use of such a compound, the claims as amended are not obvious based on the teachings of Klaus et al. singly or in view of Perrine et al.

Response:

Applicants' arguments are carefully considered but are not persuasive. Although, Klaus et al does not specifically disclose the inherent functioning of hydroxamate (iron chelator – p. 31 claim 36) or structural mimetics of 2 oxo-glutarate that inhibits HIF prolyl hydroxylase i.e. increasing expressing of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cells, Klaus et al discloses that they are inhibitors of HIF prolyl hydroxylase and teach method for treating a subject having anemia related conditions or disorders such as hemoglobinopathy such as abnormal hemoglobin such as thalassemia major and minor (beta thalassemia), sickle cell disease (sickle cell syndrome, sickle cell anemia) (p. 11 paragraph 80) with said compounds. Klaus et al discloses the same HIF prolyl hydroxylase inhibitors as claimed for treating the same condition in the claims i.e. hemoglobinopathy.

The ability of the hydroxamate or structural mimetics of 2 oxo-glutarate which are inhibitors HIF prolyl hydroxylase to increase expression of the gene encoding γ-globin in a bone marrow derived cell or hematopoietic stem cells or blast forming erythroid cell is inherent to the hydroxamate or structural mimetics of 2 oxo-glutarate. Moreover, Klaus et al teaches the same active method steps. The wherein clause " wherein the compound increases expression of the gene encoding γ-globin in a bone marrow derived cell a hematopoietic stem cell or a blast – forming unit erythroid cell" merely expresses the intended result of the positively recited step of administering the inhibitor of HIF prolyl hydroxylase to a subject and is not given any weight. See MPEP 2111.04. Thus, it would have been prima facie obvious to one of ordinary skill in the art to have used the method of Klaus et al to treat other β thalassemia disorders such as β^0- or β^+-, thus resulting in the instant invention with a reasonable expectation of success. The motivation to do so is that Klaus et al teach that hemoglobinopathy such as abnormal hemoglobin such as beta thalassemia can be treated by administering HIF prolyl hydroxylase inhibitors such as hydroxamate or structural mimetics of 2 oxo-glutarate. Moreover, as evidenced by Skarpidi et al (Experimental Hematology 31 (March 2003) 197-203, cited previously) one of skill in the art would have recognized that the hydroxamate iron chelators (which are inhibitor of hypoxia inducible factor prolyl hydroxylase as taught by Klaus et al) have the inherent property of being able to increase the level of fetal hemoglobin as well as increase the expression of the gene encoding γ-globin and Skarpidi et al teach that said hydroxamate iron chelators are potent inducers of γ-globin gene expression and Skarpidi et al suggest that these hydroxamate iron chelators for treatment of beta thalassemia and sickle cell disease (see p. 202 column 1 first incomplete paragraph and last bridging paragraph to column 2).

Status of Claims

Claims 1, 12-16 and 48-49 are rejected. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is (571)272-9939. The examiner can normally be reached on M-F 5:30 am- 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645